L4 ANSWER 1 OF 1 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2002:539680 CAPLUS
DOCUMENT NUMBER: 137:93737
TITLE: Preparation of pyridoindoles as anti-AIDS agents
INVENTOR(S): Rice, William G.; Huang, Mingjun; Buckheit, Robert W., Jr.; Covell, David G.; Czerwinski, Grzegorz; Michejda, Christopher J.
PATENT ASSIGNEE(S): The Government of the United States of America, Secretary of Health and Human Services, USA; Makarov, Vadim
SOURCE: PCT Int. Appl., 49 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002055520	A2	20020718	WO 2001-US48310	20011213
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
US 2002182151	A1	20021205	US 2001-17323	20011213

PRIORITY APPLN. INFO.: US 2000-256556P P 20001218
OTHER SOURCE(S): MARPAT 137:93737
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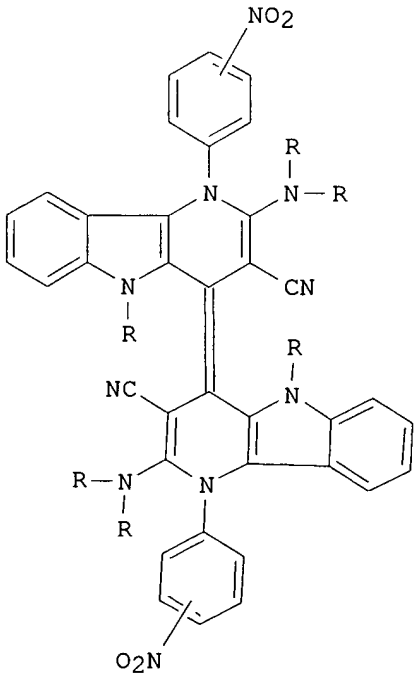

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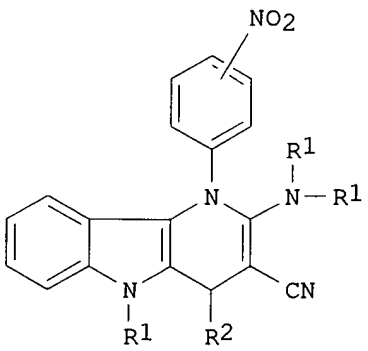

II

AB The title benzoylalkylindolepyridinium (BAIP) [sic] compds. I and II [wherein R and R1 = independently H or aliph.; R2 = CH2COCH3] were prepd. and tested for antiviral activity against several retroviruses. I inhibit the reserve transcriptase enzymes of several retroviruses, including human immunodeficiency virus (HIV). For example, deacylation of 3-(p-nitrophenylamino)indole (80%), followed by formylaton (96%) and condensation with malonitrile (80%), afforded the (aminoindolylmethylidenyl)malononitrile intermediate. Cyclization to the 2-imino-1,2-dihydro-5H-pyrido[3,2-b]indole (60%). Methylation with MeI in acetone in the presence of anhyd. K2CO3 produced the unexpected 2-oxopropyl product I (R1 = Me; R2 = CH2COCH3; p-nitrophenyl) (III). The latter exerted antiretroviral activity against HIV-1RF, HIV-2ROD, and SIV in a std. screening cytoproctection assay with EC50 values of 0.1 .mu.M, 4.79 .mu.M, and 5.65 .mu.M, resp., and CC50 values > 200 .mu.M. Further studies demonstrated that III acts during the late phase of infection, after the provirus has integrated into the host cell genome, and that cells treated with III showed reduced virion-assocd. reverse transcriptase activity and viral infectivity levels. I and II are useful for therapy to individuals already carrying HIV-1 variants that are resistant to AZT or classical non-nucleoside reverse transcriptase inhibitors (no data).

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E2            4     RICE WILLIAM E/AU
E3           57 --> RICE WILLIAM G/AU
E4            1     RICE WILLIAM GLENN/AU
E5            2     RICE WILLIAM H/AU
E6           13     RICE WILLIAM J/AU
E7            1     RICE WILLIAM JAMES/AU
E8            1     RICE WILLIAM JOHN/AU
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=> S (E3 OR E4) AND (HIV)
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          47636 HIV
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L3            1 ("RICE WILLIAM G"/AU OR "RICE WILLIAM GLENN"/AU) AND (BAIP)

=> d l3 ibib abs

L3   ANSWER 1 OF 1  CAPLUS  COPYRIGHT 2003 ACS
ACCESSION NUMBER:         2002:539680  CAPLUS
DOCUMENT NUMBER:          137:93737
TITLE:                    Preparation of pyridoindoles as anti-AIDS agents
INVENTOR(S):              Rice, William G.; Huang, Mingjun; Buckheit,
                          Robert W., Jr.; Covell, David G.; Czerwinski,
                          Grzegorz; Michejda, Christopher J.
PATENT ASSIGNEE(S):       The Government of the United States of America,
                          Secretary of Health and Human Services, USA; Makarov,
```

Vadim

SOURCE: PCT Int. Appl., 49 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002055520	A2	20020718	WO 2001-US48310	20011213
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
US 2002182151	A1	20021205	US 2001-17323	20011213

PRIORITY APPLN. INFO.: US 2000-256556P P 20001218
OTHER SOURCE(S): MARPAT 137:93737
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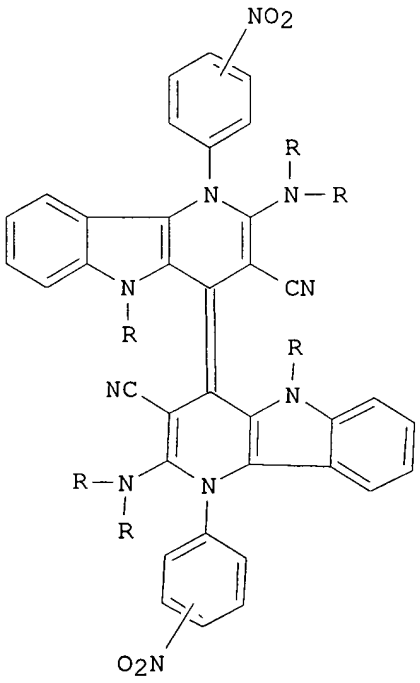

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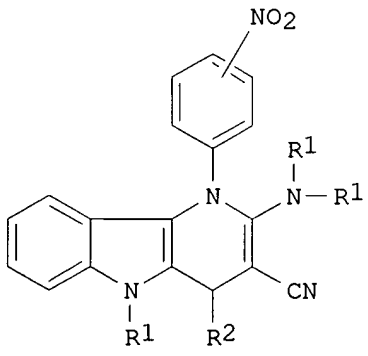

II

AB The title benzoylalkylindolepyridinium (**BAIP**) [sic] compds. I and II [wherein R and R1 = independently H or aliph.; R2 = CH2COCH3] were prepd. and tested for antiviral activity against several retroviruses. I inhibit the reserve transcriptase enzymes of several retroviruses, including human immunodeficiency virus (HIV). For example, deacylation of 3-(p-nitrophenylamino)indole (80%), followed by formylaton (96%) and condensation with malonitrile (80%), afforded the (aminoindolylmethylidenyl)malononitrile intermediate. Cyclization to the 2-imino-1,2-dihydro-5H-pyrido[3,2-b]indole (60%). Methylation with MeI in

acetone in the presence of anhyd. K_2CO_3 produced the unexpected 2-oxopropyl product I (R1 = Me; R2 = CH_2COCH_3; p-nitrophenyl) (III). The latter exerted antiretroviral activity against HIV-1RF, HIV-2ROD, and SIV in a std. screening cytoproctection assay with EC50 values of 0.1 .mu.M, 4.79 .mu.M, and 5.65 .mu.M, resp., and CC50 values > 200 .mu.M. Further studies demonstrated that III acts during the late phase of infection, after the provirus has integrated into the host cell genome, and that cells treated with III showed reduced virion-assocd. reverse transcriptase activity and viral infectivity levels. I and II are useful for therapy to individuals already carrying HIV-1 variants that are resistant to AZT or classical non-nucleoside reverse transcriptase inhibitors (no data).

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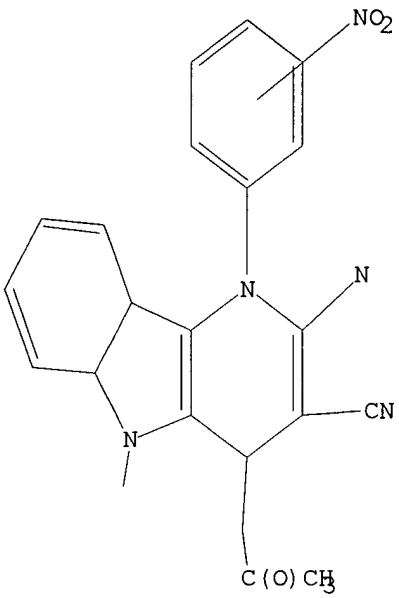

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L5 ANSWER 1 OF 2 REGISTRY COPYRIGHT 2003 ACS
RN 184772-01-8 REGISTRY
CN 1H-Pyrido[3,2-b]indole-3-carbonitrile, 2-(dimethylamino)-4,5-dihydro-5-methyl-4-(1-methyl-2-oxopropyl)-1-(4-nitrophenyl)- (9CI) (CA INDEX NAME)
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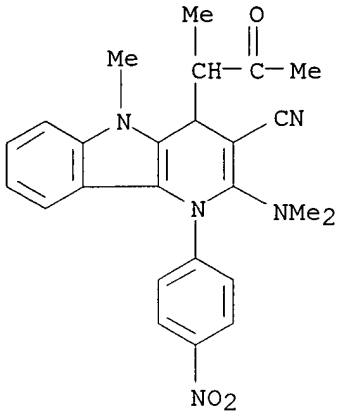

PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1 REFERENCES IN FILE CA (1962 TO DATE)
1 REFERENCES IN FILE CAPLUS (1962 TO DATE)

L5 ANSWER 2 OF 2 REGISTRY COPYRIGHT 2003 ACS
RN 167954-18-9 REGISTRY
CN 1H-Pyrido[3,2-b]indole-3-carbonitrile, 2-(dimethylamino)-4,5-dihydro-5-methyl-1-(4-nitrophenyl)-4-(2-oxopropyl)- (9CI) (CA INDEX NAME)
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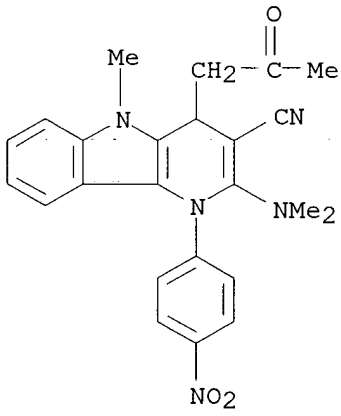

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FILE COVERS 1907 - 5 Feb 2003 VOL 138 ISS 6
FILE LAST UPDATED: 4 Feb 2003 (20030204/ED)

This file contains CAS Registry Numbers for easy and accurate substance identification.

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L6 4 L5

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L6 ANSWER 1 OF 4 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2002:575081 CAPLUS
DOCUMENT NUMBER: 137:125149
TITLE: Preparation of pyridoindoles as reverse transcriptase inhibitors.
INVENTOR(S): Rice, William G.; Huang, Mingjun; Buckheit, Robert W., Jr.; Covell, David G.; Czerwinski, Grzegorz; Michejda, Christopher J.
PATENT ASSIGNEE(S): The Government of the United States of America, Department of Health and Human Services, USA
SOURCE: PCT Int. Appl., 62 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002059123	A2	20020801	WO 2001-US48311	20011213

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 2000-256581P P 20001218
OTHER SOURCE(S): MARPAT 137:125149

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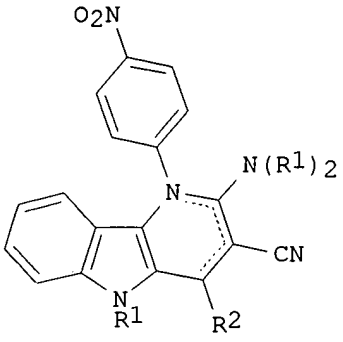

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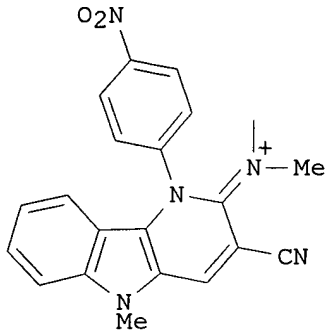
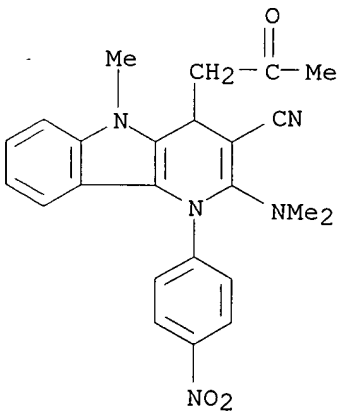


AB Title compds. (I; R1 = alkyl; R2 = H, alkyl, alkylamide, Q1; dotted lines = optional double bonds), were prepd. Thus, 1-(4-nitrophenyl)-2-methylimino-3-cyano-5-methyl-1,2-dihydro-5H-pyrido[3,2-b]indole (prepn. given) was refluxed with K2CO3, MeI, and acetone for 45 h to give 1-(4-nitrophenyl)-2-dimethylamino-3-cyano-4-(2-oxopropyl)-5-methyl-1,2-dihydro-5H-pyrido[3,2-b]indole. The latter showed IC50 = 0.1 .mu.M against HIV-1 RF in CEM-SS cells.

IT **167954-18-9P**
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of pyridoindoles as reverse transcriptase inhibitors)

RN 167954-18-9 CAPLUS

CN 1H-Pyrido[3,2-b]indole-3-carbonitrile, 2-(dimethylamino)-4,5-dihydro-5-methyl-1-(4-nitrophenyl)-4-(2-oxopropyl)- (9CI) (CA INDEX NAME)



L6 ANSWER 2 OF 4 CAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 2002:539680 CAPLUS

DOCUMENT NUMBER: 137:93737

TITLE: Preparation of pyridoindoles as anti-AIDS agents

INVENTOR(S): Rice, William G.; Huang, Mingjun; Buckheit, Robert W., Jr.; Covell, David G.; Czerwinski, Grzegorz; Michejda, Christopher J.

PATENT ASSIGNEE(S): The Government of the United States of America, Secretary of Health and Human Services, USA; Makarov, Vadim

SOURCE: PCT Int. Appl., 49 pp.
CODEN: PIXXD2
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RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
US 2002182151	A1	20021205	US 2001-17323	20011213

PRIORITY APPLN. INFO.: US 2000-256556P P 20001218
OTHER SOURCE(S): MARPAT 137:93737
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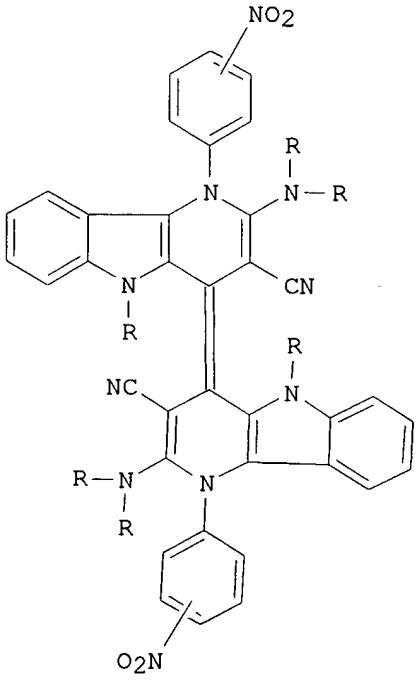

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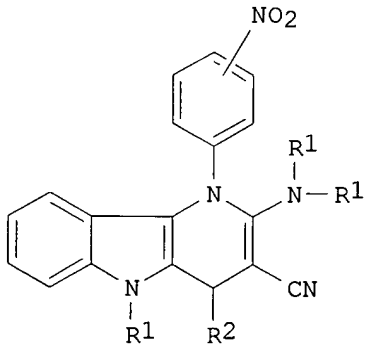

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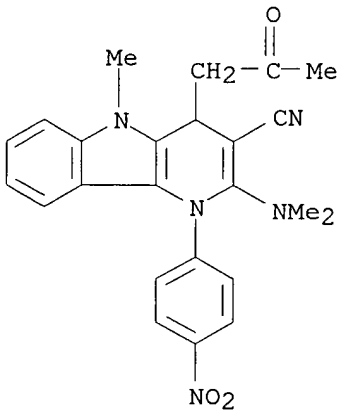
IT **167954-18-9P**

RL: ADV (Adverse effect, including toxicity); PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(antiretroviral agent; prepn. of pyridoindole anti-AIDS agents via cyclization and subsequent derivatization of (aminoindolylmethylidenyl)malononitrile)

RN 167954-18-9 CAPLUS

CN 1H-Pyrido[3,2-b]indole-3-carbonitrile, 2-(dimethylamino)-4,5-dihydro-5-methyl-1-(4-nitrophenyl)-4-(2-oxopropyl)- (9CI) (CA INDEX NAME)



L6 ANSWER 3 OF 4 CAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 1996:735136 CAPLUS

DOCUMENT NUMBER: 126:47132

TITLE: 2-Formyl-3-(arylamino)indoles in the synthesis of 1,2- and 1,4-dihydro-5H-pyrido[3,2-b]indoles (dihydro-.delta.-carbolines)

AUTHOR(S): Ryabova, S. Yu.; Alekseeva, L. M.; Granik, V. G.

CORPORATE SOURCE: TSKHLS, VNIKHFI, Moscow, Russia

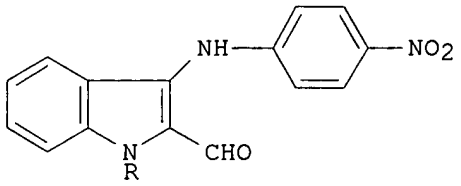
SOURCE: Khimiko-Farmatsevticheskii Zhurnal (1996), 30(9), 29-34
CODEN: KHFZAN; ISSN: 0023-1134

PUBLISHER: Izdatel'stvo Folium

DOCUMENT TYPE: Journal

LANGUAGE: Russian

GI



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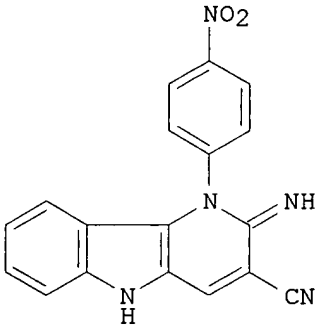

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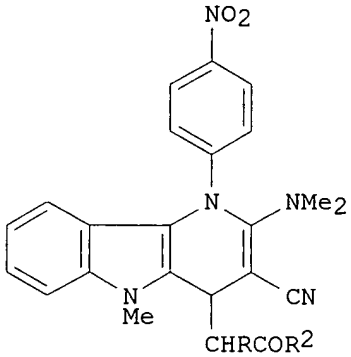


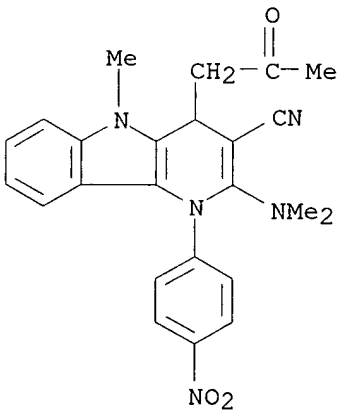
III

AB Condensation of the CHO group of title aldehydes I (R = H, Ac) with malononitrile, followed by cyclization, gave 1,2-dihydro-.delta.-carboline II, which reacted with MeI and carbonyl compds. to give 1,4-dihydro-.delta.-carbolines III [R = H, R1 = Me; RR1 = (CH2)4; R = R1 = Me].

IT **167954-18-9P 184772-01-8P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of)

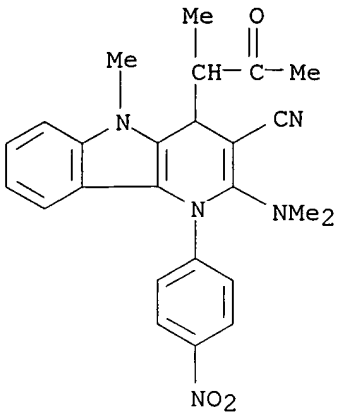
RN 167954-18-9 CAPLUS

CN 1H-Pyrido[3,2-b]indole-3-carbonitrile, 2-(dimethylamino)-4,5-dihydro-5-methyl-1-(4-nitrophenyl)-4-(2-oxopropyl)- (9CI) (CA INDEX NAME)



RN 184772-01-8 CAPLUS

CN 1H-Pyrido[3,2-b]indole-3-carbonitrile, 2-(dimethylamino)-4,5-dihydro-5-methyl-4-(1-methyl-2-oxopropyl)-1-(4-nitrophenyl)- (9CI) (CA INDEX NAME)

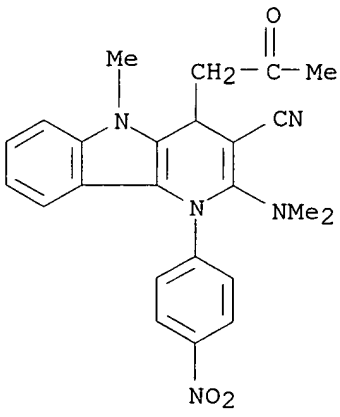


L6 ANSWER 4 OF 4 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1995:622244 CAPLUS
DOCUMENT NUMBER: 123:198747
TITLE: A new approach to the synthesis of 1,2- and 1,4-dihydropyrido[3,2-b]indole derivatives
AUTHOR(S): Ryabova, Svetlana Yu.; Alekseeva, Lyudmila M.; Granik, Vladimir G.
CORPORATE SOURCE: Cent. Medicinal Chem., All-Russian Res. Chem.-Pharmaceutical Inst., Moscow, 119815, Russia
SOURCE: Mendeleev Communications (1995), (3), 107-9
CODEN: MENCEX; ISSN: 0959-9436
PUBLISHER: Russian Academy of Sciences
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 123:198747

AB Intramol. cyclization of .alpha.-cyano-.beta.-(3-p-nitrophenylaminoindol-2-yl)acrylonitrile yields 1-p-nitrophenyl-2-imino-3-cyano-1,2-dihydropyrido[3,2-b]indole, methylation of which by Me iodide in acetone in the presence of potassium carbonate is accompanied by the addn. of acetonyl anion and formation of 1-p-nitrophenyl-2-dimethylamino-3-cyano-4-acetonyl-1,4-dihydropyrido[3,2-b]indole.

IT **167954-18-9P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of dihydropyrido[3,2-b]indoles)

RN 167954-18-9 CAPLUS
CN 1H-Pyrido[3,2-b]indole-3-carbonitrile, 2-(dimethylamino)-4,5-dihydro-5-methyl-1-(4-nitrophenyl)-4-(2-oxopropyl)- (9CI) (CA INDEX NAME)



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